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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,880	10/12/2000	Austin G. Smith	06999.0009	5994

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/21/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/686,880	Applicant(s) SMITH ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 42-65 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 42-54,58,64 and 65 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 55-57 and 59-63 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' preliminary amendment filed 10-12-00 and supplemental amendment filed 6-19-01 have been entered. Claims 1-41 have been canceled. Claims 42-65 are pending.

This application is a continuation of PCT/GB99/01136, filed 10-14-99, and claims priority of foreign application United Kingdom 98-7935.3, filed 4-14-98.

1. Applicant's election of group I, claims 42-54, 58, 64 and 65, in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.E.P.. § 818.03(a)).

2. Claims 55-57 and 59-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12.

Priority

3. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a continuation of Application No. PCT/GB99/01136, filed 10-14-99." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom 98-7935.3 on 4-14-98. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Specification

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Oath/Declaration

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See M.E.P.. §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor.

It does not identify the city and state or foreign country of residence of each inventor.

It does not include the inventors' signature.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 47-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "according to **any** of claim 42" in claims 47-49 is vague and renders the claims indefinite. Claim 42 is only one claim and it is unclear whether there is any claim other than claim 42 to be depended from. Claims 50 and 51 depend on claim 49 but fail to clarify the indefiniteness.

The phrase "a culture substantially of individual cells" in claim 50 is vague and renders the claim indefinite. It is unclear as to the metes and bounds of what would be considered "substantially". The specification fails to specifically define the term "substantially".

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 42-54, 58 and 65 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Li et al., 1998 (Current Biology, Vol. 8, p. 971-974-IDS).

Claims 42-54, 58 and 65 are directed to a method for generating a purified or enriched culture of neural progenitor cells by introducing into a multipotential cell, such as ES cells, EG cells, EC cells, a primary culture of fetal cells etc., a selectable marker, such as antibiotic resistance gene, deferentially expressed in cells of the selected lineage compared with its expression in other cells, culturing the multipotential cell *in vitro* to induce differentiation of the multipotential cell into a cell of the selected lineage, and selecting for cells of the selected lineage according to differential expression of the selectable marker. Claim 45 specifies genetically modifying multipotential cells to delete, mutate or add genes to study gene function. Claims 46 specifies adding a second selectable marker to identify sub-lineage cells from the cells of selected lineage. Claims 47 and 48 specify the selectable marker is introduced into the multipotential cells via targeted integration or random gene trap integration. Claims 53 and 54 specify the selectable marker is expressed in cells that express a Sox gene, such as Sox 1, Sox 2, or Sox 3.

Li teaches a method of isolating neural progenitor cells by introducing a bifunctional selection marker/receptor gene βgeo into ES cells and said βgeo gene integrated into Sox 2 gene via homologous recombination, and G418 is added after retinoic acid induction, either during embryoid body culture or upon plating, to select neural progenitor cells expressing Sox 2 (e.g. p. 971, 972). Li further teaches using a second selection marker, such as the bHLH transcription factors Mash1 and Math4A, that defines distinct subpopulations of neural progenitors to select subpopulation cells of the selected neural progenitors (e.g. p. 972, right column). Li also suggests that "This ability to generate pure populations of neurons, combined with the relative

ease of genetic modification of ES cells, offers a new route for manipulation and characterization of neuronal development and cell biology" (e.g. p. 973, left column). Thus, claims 42-54, 58 and 65 are clearly anticipated by Li.

It should be noted that a certified copy of the claimed foreign application United Kingdom 98-7935.3, filed 4-14-98, has not been received. Therefore, the claimed foreign priority of United Kingdom 98-7935.3 is not granted. Thus, claims 42-54, 58 and 65 are rejected under 35 U.S.C. 102 (b).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 42 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al., 1998 (Current Biology, Vol. 8, p. 971-974-IDS) in view of Meryman, 1997 (US Patent No. 5,629,145).

Claims 42 and 64 are directed to a method of preparing a neural progenitor cell or a differentiated progeny thereof for storage by freezing the progenitor cells in the presence of a cryoprotectant.

Li teaches a method of isolating neural progenitor cells by introducing a bifunctional selection marker/receptor gene βgeo into ES cells and said βgeo gene integrated into Sox 2 gene via homologous recombination, and G418 is added after retinoic acid induction, either during embryoid body culture or upon plating, to select neural progenitor cells expressing Sox 2 (e.g. p. 971, 972). Li further teaches using a second selection marker, such as the bHLH transcription factors Mash1 and Math4A, that defines distinct subpopulations of neural progenitors to select subpopulation cells of the selected neural progenitors (e.g. p. 972, right column). Li does not teach storage of cells by freezing cells with cryoprotectant.

Meryman teaches a method for cryopreservation of a cell suspension comprising mixing said cell suspension with a storage solution containing at least one non-penetrating polymer or cryoprotectant, such as dextran or hydroxyethyl starch, and freezing the cells at a temperature between T_{hom}, spontaneous freezing temperature of intracellular solution, and T_g, glass transition temperature, to avoid ice nucleation of intracellular solution, and to prevent cell injury during freezing process and to prolong shelf-life of cellular products (e.g. column 3, 6, 8).

It would have been obvious for one of ordinary skill at the time of the invention to store cells by freezing cells with the presence of cryoprotectant because of the teachings of Meryman and it was general knowledge and practice to store cells by freezing said cells with a cryoprotectant.

One having ordinary skill at the time the invention was made would have been motivated to do so in order to store the cells for future use and to prolong shelf-life of cellular products as taught by Meryman. Thus, claims 42 and 64 are rejected under 35 U.S.C. 103(a).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Kimberly Davis, whose telephone number is (703) 305-3015.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.